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Review article – *Special issue: Imaging in Coronary Artery Disease*

Coronary CT angiography

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ABSTRACT

Coronary CT angiography (coronary CTA) represents an increasingly applied noninvasive method for coronary artery imaging. Due to technical development and improved spatial and temporal resolution of CT, high diagnostic value of coronary CTA is reported when compared to conventional selective angiography. The aim of this review is to present an overview of the clinical applications of coronary CTA. Important factors in patient selection and preparation are also briefly discussed.

Contents

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Introduction

Coronary artery disease (CAD) is the leading cause of morbidity and mortality in developed countries [1]. Invasive selective coronary angiography was the only method to image coronary arteries for a long time and is still the gold standard [2]. However, technology allowing nonivasive imaging by coronary CT angiography (coronary CTA) has progressed remarkably during the last three decades. Harrel and his research group laid the groundwork for cardiac CT already in 1976 and 1979 [3]. The basic principles of their reconstruction technique and particularly their method of obtaining a short snapshot of the heart are still applied today in what is now known as multisegment reconstruction [3]. It took more than two decades of research after Harrel's initial experiment to develop CT scanners suitable for routine cardiac imaging. The introduction of 16-slice CT in 2003 and 64-slice CT in 2004 marked the arrival of technology with sufficient spatial and temporal resolution for assessment of coronary arteries [4]. Today, only ≥64-slice CT is considered to be appropriate for coronary artery imaging.

Basic aspects of image acquisition

Coronary CTA has some specific technical aspects which need to be briefly addressed. CT imaging of the heart requires minimization of cardiac motion artifacts. For this reason, coronary CTA scanning is performed with simultaneous ECG registration. Two basic methods are recognized: prospective triggering and retrospective gating. Prospective ECG triggering is a method in which the data are acquired at a pre-specified phase of the cardiac cycle. For coronary CTA, the phase with minimal heart motion and therefore minimal coronary artery motion (usually in mid-diastole or in end-systole in patients with an accelerated heart rate) is selected. In retrospective ECG gating, data are acquired throughout the entire cardiac cycle, and only the data obtained during the cardiac phase with the least motion artifacts are used for image reconstruction. The protocol for cardiac CT is highly dependent on the technology delivered by each vendor. Some vendors attempt to decrease the radiation dose by prospective triggering and fast rotation times, while others build their protocols mainly on helical scanning and ECG pulsing, where full dose images are acquired only during a pre-selected phase. Prospective ECG triggering is being performed more frequently in recent years because of its relatively low radiation dose (2–6 mSv) in comparison with the retrospective gating or pulsing methods (6–20 mSv). However, the most important disadvantage of prospective triggering lies in the fact that images can be reconstructed only for a pre-selected phase of the cardiac cycle, and functional assessment of the heart (e.g. assessment of left ventricular ejection fraction) is thus not feasible. All coronary CTAs are contrast examinations. Image quality depends on the contrast-to-noise ratio, and therefore high concentration iodine (e.g. 350 mg/ml or 400 mg/ml) contrast agents are preferred. Contrast volume ranges from 50 to 100 ml. The required injection rate is typically between 4 and 7 ml/s and so adequate intravascular access (20 gauge or 18 gauge intravenous cannula placed typically in the right antecubital vein is usually used) is needed. Optimal images require high intra-arterial opacification of more than 250 Hounsfield units (HU). Vascular enhancement should be maintained for the duration of data acquisition; therefore accurate timing of the scan is necessary. For this purpose, either the bolus tracking or the test bolus technique can be used. The bolus tracking technique is based on automatic scan triggering. In this strategy, the region of interest (left atrium, ascending or descending aorta) is selected and is sampled every 1–2 s after the initiation of contrast agent administration. When the density in the selected region exceeds target density value (e.g. 100 HU), scanning is started. In the test bolus strategy, a small test bolus is administered, and sampling is performed at the region of interest every 1–2 s, allowing measurement of the time to contrast arrival. This time is then used to trigger the scan acquisition once the full contrast dose has been administered.

Patient preparation

The following set of recommendations is usually given to the patient undergoing coronary CTA [5]: (1) no food intake for 4 h before the examination; (2) drinking of water or clear fluids up until time of the examination is not restricted and is even encouraged, mainly to improve hydration of the patient in order to prevent renal impairment caused by contrast agent administration and also for the ease of establishing venous access; (3) caffeine products should be restricted 12 h before examination, as they might hinder efforts to reduce the heart rate before scanning; (4) regular blood pressure medication, particularly heart rate lowering drugs, should not be discontinued prior examination; (5) pre-medication for contrast allergy as prescribed by the referring physician; (6) metformin discontinuation for 48 h after examination is usually advised although this recommendation seems to be nowadays rather

questionable; (7) in subjects with heart rate ≥65/min, rate-controlling drugs like beta blockers and other drugs with negative chronotropic properties, such as ivabradine [6] and verapamil, are administered in order to achieve a target heart rate of 50–60 beats/min to minimize motion artifacts (at our institution 50–300 mg of short-acting esmolol is administered intravenously immediately prior to scanning); (8) sublingual administration of nitrates a few minutes before the initiation of the scan protocol is recommended in patients without contraindication, in order to improve visualization of the coronary arteries.

Patient selection

Appropriate selection of patients who should benefit from coronary CTA is of utmost importance. The list of indications that are currently considered to be appropriate according to the recommendations of the Society of Cardiovascular Computed Tomography and other expert societies [7] is shown in Table 1. However, not all patients with an appropriate clinical indication are suitable for coronary CTA. It is mandatory that patients undergoing coronary CTA are able to cooperate with instructions to be motionless, supine, and to hold their breath during the imaging [8]. Subjects with a rapid heart rate (≥100 beats/min), particularly with irregular R–R intervals such as in atrial fibrillation, are also not suitable candidates for coronary CTA. Until recently, irregular heart rates >80 beats/min represented a relative contraindication for coronary CTA because of the high incidence of motion artifacts [4]. However, ongoing hardware and software development and improvements, such as ≥64-slice CT, wide-detector scanners, or dual-source CT, now allow the scanning of patients with higher and irregular heart rates with sufficient imaging quality. Therefore, the decision, whether the examination of the patient with higher heart rate will be performed, depends not just only on the patient's heart rate but also on the available CT equipment. Moreover, patients with a higher heart rate or significant heart rate variability (e.g. >5 beats/min) are not well-suited for a prospectively ECG-triggered technique and thus often require a retrospective ECG gating method with a significantly higher radiation dose [9].

Table 1 – Appropriate indications for coronary CTA according to the recommendations of the Society of Cardiovascular Computed Tomography [7].

1) Detection of CAD in symptomatic patients without known ischemic heart disease
A) Patients with nonacute presentation and symptoms possibly representing an ischemic equivalent
- low pretest probability of CAD and ECG uninterpretable or unable to exercise
- intermediate pretest probability of CAD and ECG interpretable and able to exercise
- intermediate pretest probability of CAD and ECG uninterpretable or unable to exercise
- normal ECG exercise test and continued symptoms
- discordant ECG exercise test and imaging results
- equivocal stress imaging results
B) Patients with acute presentation and suspicion of ACS
- low pretest probability of CAD and normal ECG and cardiac biomarkers
- low pretest probability of CAD and nondiagnostic ECG or equivocal cardiac biomarkers
- low pretest probability of CAD and ECG uninterpretable
- intermediate pretest probability of CAD and normal ECG and cardiac biomarkers
- intermediate pretest probability of CAD and nondiagnostic ECG or equivocal cardiac biomarkers
- intermediate pretest probability of CAD and ECG uninterpretable
2) Detection of CAD in patients with new-onset or newly diagnosed HF and no prior CAD
- low or intermediate probability of CAD and reduced left ventricular ejection fraction
3) Detection of CAD in patients undergoing noncoronary cardiac surgery
- intermediate pretest probability of CAD
4) Risk assessment after CABG
- evaluation of graft patency in patients with symptoms possibly representing ischemic equivalent
- localization of graft prior to reoperative chest or cardiac surgery
5) Risk assessment after PCI in asymptomatic patients
- prior left main PCI with stent diameter ≥3 mm
6) Assessment of anomalies of coronary arteries

CAD, coronary artery disease; HF, heart failure; PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting.

Coronary CT in clinical applications

Suspected stable coronary artery disease

The most obvious indication for cardiac CT is to exclude CAD in patients with symptoms possibly representing an ischemic equivalent with low-to-intermediate pretest probability of CAD. Other clinical scenarios include patients with low-to-intermediate pretest probability of CAD and new-onset or newly diagnosed heart failure with reduced left ventricular ejection fraction, as well as subjects undergoing noncoronary cardiac surgery with intermediate pretest probability of CAD. Numerous single and multicenter studies have addressed the diagnostic value of coronary CTA in detecting stenoses of coronary arteries [10–12]. Based on the results of so far published studies particularly very good negative predictive value was highlighted (Fig. 1). In very recent meta-analysis performed by Menke and Kowalski including 30 studies (3422 patients) published between 2005 and 2013, diagnostic performance of coronary CTA was assessed and the findings were compared with invasive selective coronary angiography representing the gold standard in imaging of coronary arteries [13]. Most studies (22 studies with 2593 patients) in this meta-analysis applied ≥64-slice CT or dual-source CT. About 6% of coronary CTA examinations were unevaluable. Even considering unevaluable results, the pooled sensitivity of coronary CTA was 93.9% and specificity 79.2%. Sensitivity and specificity were even higher in the subgroup of patients examined by ≥64-slice CT (95.6% and 81.5%).

On the other hand, patients with high pretest likelihood of CAD (e.g. older men or women with typical angina pectoris) should not undergo coronary CTA for exclusion of CAD as the first-line imaging method, because more patients in this subgroup would require invasive selective coronarography as

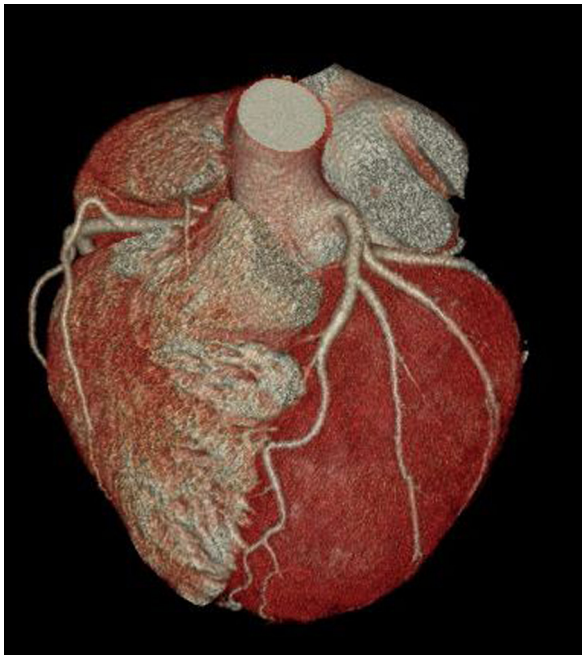

Fig. 1 – Three-dimensional volume-rendered CT image depicting normal coronary arteries.

the negative predictive value of coronary CTA is reduced and thus negative coronary CTA results are less reliable.

Suspected acute coronary syndrome

Coronary CTA represents an alternative to conventional selective angiography in patients with suspected acute coronary syndrome (ACS), who have low or intermediate pretest probability of CAD and their ECG is either normal or non-diagnostic, and cardiac biomarkers are normal or equivocal. Four randomized trials, CT-STAT [14], ACRIN-PA [15], ROMICAT II [16] and CT-COMPARE [17], have compared a strategy based on coronary CTA to the standard of care in evaluation of over 3000 patients with suspected ACS with low-to-intermediate risk. These trials consistently demonstrated the safety of negative coronary CTA results in identifying patients for discharge from the emergency department with very low rates (<1%) of major adverse cardiovascular events, at significantly lower cost, and greater efficiency in terms of time to discharge and length of hospital stay [18].

Coronary plaques

Atherosclerotic plaques start accumulating long before the development of luminal stenoses and the early stages of coronary plaques are typically associated with the outer expansion of the wall (positive remodeling of the vessel) [19]. Even this early stage of atherosclerosis is known to be associated with increased risk of the cardiovascular events. Because coronary CTA has the ability to simultaneously assess luminal dimensions and the vessel wall, it can detect these early disease stages, which are not well visualized by invasive coronary angiography. In coronary CTA examination, plaques are usually classified according to the presence or absence of calcified components, thereby differentiating between calcified, partially calcified (mixed), and non-calcified plaques [20] (Fig. 2). However, subclassification of non-calcified plaques to lipid-rich and fibrous lesions based on the values of CT attenuation cannot be easily applied. Although the density of plaques measured by CT correlates with echogenicity determined by intravascular ultrasound, there is significant overlap of attenuation values between the different non-calcified plaques types. Despite the challenges associated with classification of plaques based on CT attenuation, there is evidence that low density plaques (<30 HU) are more often seen in patients with ACS than those with stable CAD, and that these plaques are more often associated with a ruptured fibrous cap of the culprit lesion [21]. The effect of calcification on plaque instability is controversial. While heavily calcified plaques are relatively stable, plaques containing small (<1 mm) spotty calcifications are associated with accelerated disease progression and are one of the features of vulnerable plaques [22]. Moreover, the napkin-ring sign is considered to be a specific CT feature of plaques with large necrotic core and thus represents a reliable marker of plaque instability. The napkin-ring sign is a qualitative plaque feature which can be defined in a non-calcified plaque cross-section by the presence of two features: a central area of low CT attenuation that is apparently in contact with the lumen and a ring-like higher attenuation plaque tissue surrounding this central area [20].

Coronary anomalies

The prevalence of coronary anomalies varies widely depending on the literature source. Anomalies of origin, course and termination can be distinguished [23]. From the clinical perspective anomalous origin of the right or left coronary artery from an inappropriate sinus is of clinical importance (Fig. 3). The prevalence of this pathology is approximately 1%

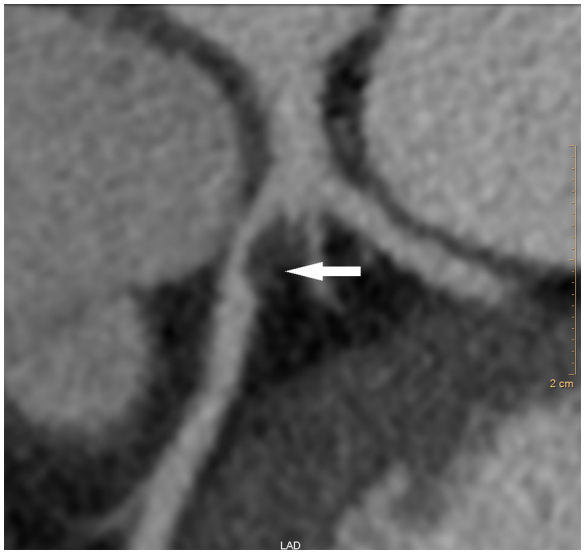

Fig. 2 – Large noncalcified plaque in the proximal left anterior descending coronary artery is shown on coronary CT angiography.

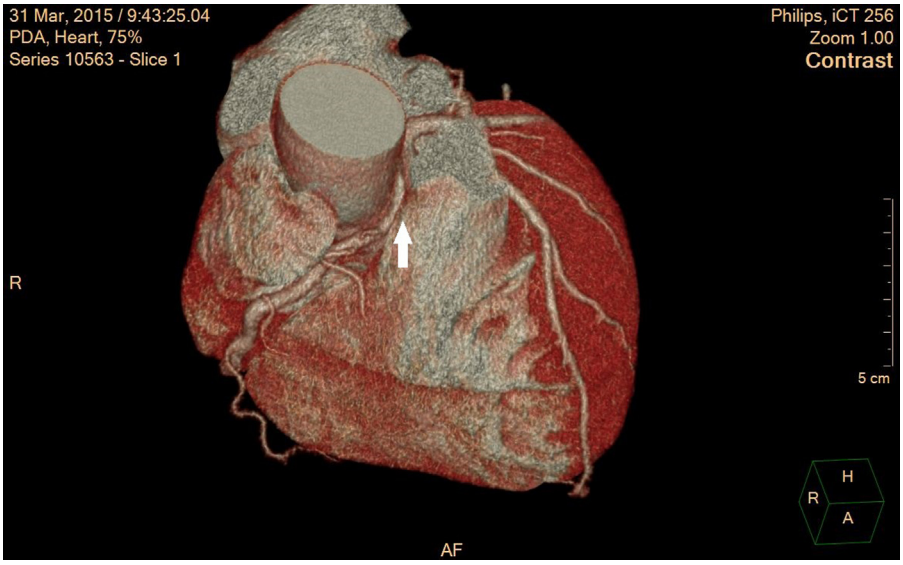

Fig. 3 – Three-dimensional volume-rendered CT image showing an interarterial course of the right coronary artery originating from the left sinus of Valsalva.

[24]. These anomalies are known to be associated with increased risk of sudden cardiac death when the coronary artery has an interarterial course between the aorta and pulmonary artery. The major advantage of coronary CTA in the diagnostic workup of a suspected coronary anomaly is better anatomic depiction of the origin and course of the coronary artery. Coronary CTA is either performed as a first line method or after conventional selective coronarography either because the latter could not detect a coronary artery or because the course of the anomalous coronary artery was not clear from the invasive coronary angiography.

Coronary artery bypass grafts (CABG)

In patients who underwent surgical revascularization of the myocardium, recurrence of symptoms can be due to graft stenosis or occlusion, or due to progression of atherosclerosis in the native vessels. In general, imaging of venous grafts is less challenging than imaging of the native coronary arteries because they are usually of larger size and have reduced mobility. Assessment of internal mammary artery grafts can be more difficult due to artifacts caused by metal clips and because of their smaller diameter. Evaluation of the distal graft anastomosis is sometimes challenging due to the frequent presence of calcifications or clips at the site and due to greater motion of this portion of the graft. Nevertheless, diagnostic performance in detecting graft stenosis or occlusion is usually excellent with sensitivity and specificity exceeding 95% [25] (Fig. 4). However, the investigation of the native coronary arteries is often very difficult because of pronounced atherosclerotic involvement and especially because of severe calcifications. Therefore, the diagnostic yield of coronary CTA in assessment of native coronary vessels in this subgroup of patients is frequently decreased and the number of unevaluable segment is relatively high.

Coronary artery stents

In most patients with significant CAD, percutaneous coronary intervention comprises placement of a stent rather than angioplasty alone (Fig. 5). The evaluation of stents is more challenging than the assessment of native coronary arteries. Several types of artifacts can complicate the evaluation of

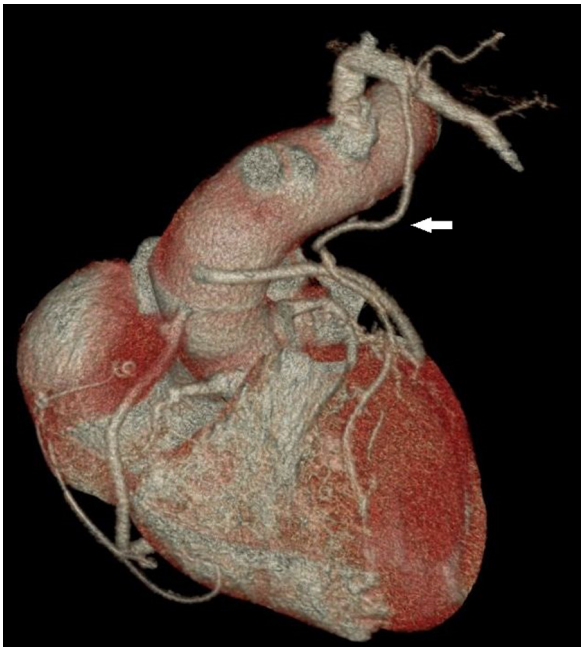

Fig. 4 – Three-dimensional volume-rendered CT image depicting normal left internal mammary bypass graft to the left anterior descending coronary artery (marked with arrow), as well as a normal venous bypass graft to the obtuse marginal artery.

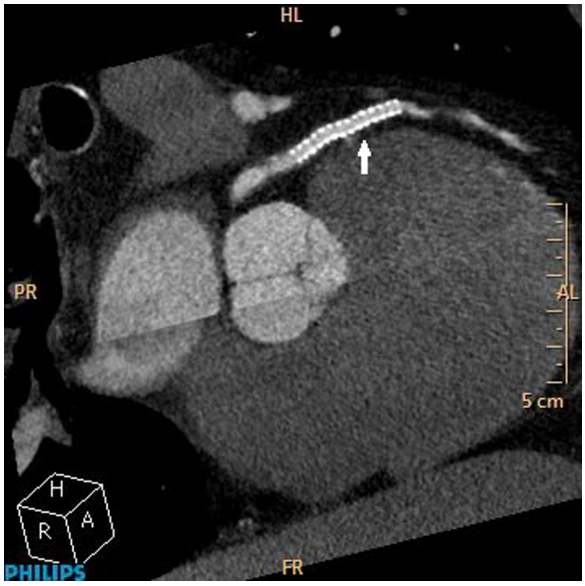

Fig. 5 – Curved multiplanar reformation demonstrating stent without restenosis in the left anterior descending artery.

Fig. 6 – Decreased attenuation in the subendocardial layer of the inferior wall corresponding to prior myocardial infarction.

coronary stents (e.g. beam hardening can lead to a virtual loss of CT density along the stent and black streaks may occur in the vessel lumen; partial volume artifact can be associated with a loss of the sharp edge delineating the stent and the lumen). Overall, the diagnostic accuracy is better in stents with diameter ≥3 mm [26]. When coronary CTA was used to evaluate in-stent restenosis using intravascular ultrasound as the reference standard, the sensitivity was 67% and specificity 78% for stents with diameter <3 mm, whereas for stents with diameter ≥3 mm it was 89% and 100%. Moreover, the diagnostic performance of coronary CTA has been found to be superior in stents with thinner struts (<100 μm) compared to stents with thicker struts [27]. Because of the limitations of coronary CTA only evaluation of stents in left main coronary artery in asymptomatic individuals is considered clearly appropriate.

Contemporary directions

Coronary CTA tends to overestimate stenoses in patients with CAD and lacks functional information about the hemodynamic significance of borderline stenoses. Thus, a combined anatomic and functional assessment of CAD seems to be of great importance. This can be achieved by combination of coronary CTA with myocardial CT perfusion (myocardial CTP) (Fig. 6) or with fractional flow reserve-CT (FFR-CT).

Stress myocardial CTP is based on evaluation of myocardial attenuation after application of coronary vasodilatating drugs like adenosine, dypiridamole, or regadenoson. Very recently, a large multicenter, prospective study exploring the accuracy of combined coronary CTA and myocardial CTP in the detection of flow-limiting stenoses (as assessed by the combination of invasive coronary angiography and single photon emission CT representing the reference methods) was published [28]. In a per-patient analysis, the accuracy of coronary CTA alone was 69% compared to 75% for the combination of coronary CTA and myocardial CTP, while in a per-vessel analysis, the accuracy of coronary CTA alone was 73%, and increased to 79% when combination of coronary CTA and myocardial CTP was applied.

FFR-CT is a novel technology that enables determination of the functional significance of lesions noninvasively, using sophisticated computer algorithms based on computational fluid dynamics applied to coronary CTA [29]. There is evidence from several randomized studies, comparing FFR-CT with invasive FFR (representing the gold standard), that FFR-CT can be helpful in evaluation of hemodynamic significance of stenosis, especially in patients with intermediate severity stenosis [30].

Conclusions

Coronary CTA represents the only reliable noninvasive alternative method to conventional selective coronary angiography for coronary artery imaging. This diagnostic method is especially useful in evaluation of subjects with suspected CAD and low-to-intermediate pretest probability. The combination of coronary CTA with myocardial CTP or FFR-CT seems to be promising.

Conflict of interest

No conflict of interest.

Ethical statement

I declare, on behalf of all authors, that the research was conducted according to Declaration of Helsinki.

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